



## Potential Early Indicator of Kidney Injury Identified



A guidance cue that helps kidneys form may also be a red flag that they are in danger, researchers report.

Acute kidney injury, a common and serious complication of hospitalization, is on the increase worldwide, affecting an estimated 6 percent of all hospitalized patients and 30-40 percent of adults and children having cardiopulmonary bypass surgery.

About 10-15 percent of acute injuries translate to chronic kidney damage or failure that may require dialysis or a kidney transplant, said Dr. Ganesan Ramesh, kidney pathologist in the Vascular Biology Center at the Medical College of Georgia at Georgia Regents University.

Now, animal and human studies have shown that within a few hours of injury, a significant amount of the protein semaphorin 3A is detectable in the urine, Ramesh and his colleagues report in the journal *PLOS ONE*.

"Semaphorin 3A appears to be a sensitive biomarker that we believe will give physicians an early and accurate heads-up that their patient's kidneys have been injured so that damage can be minimized and potentially reversed with rapid intervention," said Ramesh, the study's corresponding author.

The protein, which is not usually measurable in urine, was quickly detected in a group of 60 pediatric patients following cardiopulmonary bypass surgery at Cincinnati's Children's Hospital. High levels of the protein were about 90 percent accurate at identifying the 26 children with acute kidney injury. In those patients, urine levels were high within two hours, peaked at six hours and essentially normalized 12 hours after surgery.

Probably because of the kidney's significant reserve capacity, it's more like 48 hours before the current biomarker creatinine, a byproduct of muscle metabolism typically excreted by the kidneys, is elevated in the blood. By then, it's often too late for strategies such as massive fluid volumes, antibiotics and other interventions to yield significant improvement, he said.

In the study group, creatinine levels were essentially the same in all 60 children for 24 hours. By 48 hours, levels were significantly elevated in the acute kidney injury group and stayed up for five days.

The researchers initially identified semaphorin 3A in an animal model of temporarily compromised oxygen levels, or ischemia, to the kidneys. When they eliminated the protein's expression in a mouse, it reduced ischemia-related kidney damage.

The hard-working, high-energy kidneys are particularly vulnerable to any decreases in the usual oxygen levels that may result from life-saving strategies such as cardiopulmonary bypass and mechanical ventilation, Ramesh said. Over the course of the day, the kidneys filter the body's total blood volume several times, resorbing needed components like nutrients and eliminating toxins, excess sodium and more. When they stop filtering properly, the body starts dumping both good and bad products into the urine.

Children with congenital heart defects who need multiple surgeries to repair their hearts may be at particular risk for acute kidney injury. In the study, children who developed the injury spent the longest time on bypass and in the hospital.

Many unknowns persist about semaphorin 3A including the role of the guidance cue in the healthy developed kidney and why its levels shoot up then drop down so dramatically with injury. He notes that there is fairly significant cell turnover in the kidneys so it may have a role in regeneration. Ramesh has already worked with Japanese physicians to look at the levels in 350 older patients in intensive care for a variety of maladies. He's also working on an antibody that will screen specifically for semaphorin 3A.

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